REMARKS

Claims 1, 3-5, 8-10 and 12 are pending in the subject application. Applicant has hereinabove canceled claim 10 and amended claims 1 and 8. Accordingly, upon entry of this Amendment, claims 1, 3-5, 8-9 and 12 will be pending and under examination.

In making these amendments, applicant neither concedes the correctness of the Examiner's rejections in the May 8, 2003 Office Action, nor abandons the right to pursue in a continuing application embodiments of the instant invention no longer claimed in this application. Applicant maintains that these amendments to the specification and claims do not raise any issue of new matter, and that these claims are fully supported by the specification as originally filed. Accordingly, applicant respectfully requests that this amendment be entered.

In view of the arguments set forth below, applicant maintains that the Examiner's objections and rejections made in the May 8, 2003 Office Action have been overcome, and respectfully requests that the Examiner reconsider and withdraw same.

Rejection Under 35 U.S.C. §112, First Paragraph - Enablement

The Examiner rejected claims 1, 3-5, 8-10 and 12 under 35 U.S.C. §112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to enable one skilled in

the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

In response, but without conceding the correctness thereof, applicant notes that claim 10 has been canceled. Thus, the Examiner's rejection of this claim is now moot.

In response to the rejection of claims 1, 3-5, 8-9 and 12, applicant respectfully traverses.

The Examiner notes that the specification does not reasonably provide enablement for the broader scope of any immortalized human cardiomyocyte cell line. Specifically, the scope of immortalized human cardiomyocyte cell lines recited in the preamble of claims 1 and 3-5 is not limited, and could be construed to embrace differentiated cardiomyocytes that express action potentials and display a beating phenotype.

In response, without conceding the correctness of the Examiner's position, applicant notes that amended claim 1 contains language which fully addresses the Examiner's stated concern. Thus, the Examiner's remarks are inapposite to the claims as amended, and the claimed invention is enabled.

The Examiner also states that the instant specification teaches no example of any differentiated immortalized human cardiomyocyte and fails to provide the guidance that is missing from the prior art as to how to cause the exemplified cells to differentiate. The Examiner also asserts that the evidence of record, namely Makino, et

al. (J. Clin. Invest., 103(5): 697-705 (1999)), Leiden (J. Clin. Invest., 103(5):591-592 (1999)) and Wang et al. (In Vitro Cellular and Developmental Biology, 27(1): 63-74, 1/1991), indicates that human cardiomyocytes expressing SV-40 large T antigen cannot differentiate into committed cardiomyocytes. Therefore, one of skill in the art would allegedly have to perform undue experimentation in order to make immortalized human cardiomyocytes that express SV-40 large T antigen and that can be differentiated to beat, display action potentials, and display other characteristics of differentiated cardiomyocytes such as the expression of alpha actinin, and cardiomyocyte-specific transcription factors.

In response, applicant again respectfully traverses the Examiner's rejection. Applicant neither concedes nor denies the Examiner's above assertion. However, assuming solely for the sake of argument that human cardiomyocytes expressing SV-40 cannot differentiate into committed cardiomyocytes, applicant respectfully points out that methods to silence SV-40 gene expression for the purpose of inducing the claimed cell line to differentiate were known in the art at the time of filing. One such known method is RNA interference (RNAi) as evidenced in Fire et al. (Nature, 391:806-811 (1998)). (EXHIBIT 2). This reference teaches RNAi and its success by using double-stranded RNA to knock out expression of targeted genes, such as *unc-22*, *unc-54*, *fem-1* and *hlh-1*, in living cells. (See pages 807-809). With RNAi, a person skilled in the art at the time of filing, and in view of the instant application, would have been able to silence SV-40 gene

expression in the claimed cell line, thereby inducing the claimed cell line to differentiate without undue experimentation. Hence, with this known technology at the time of filing, one skilled in the art could have caused the claimed cell line to differentiate into committed cardiomyocyte. Therefore, the claimed invention is enabled.

The Examiner further asserts that the specification does not provide enablement for methods of making immortalized cell lines using replicable vectors conferring immortality other than vectors that express oncogenes that immortalize fibroblasts. Specifically, according to the Examiner, the scope of replicable nucleic acid vectors that can immortalize cells is not limited in claims 1, 3-5, 8-10 and 12.

In response, without conceding the correctness of the Examiner's position, applicant notes that amended claims 1 and 8 contain language which fully addresses the Examiner's stated concern. Thus, the Examiner's remarks are inapposite to the claims as amended, and the claimed invention is enabled.

In view of the above remarks, applicant maintains that claims 1, 3-5, 8-9 and 12 satisfy the requirements of 35 U.S.C. §112, first paragraph.

Rejection Under 35 U.S.C. §112, First Paragraph - Written Description

The Examiner rejected claims 1, 3-5, 8-10 and 12 under 35 U.S.C. §112, first paragraph, as allegedly containing

subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time of the application was filed, had possession of the claimed invention. Specifically, the Examiner states that the claimed invention embraces the genus of replicable vectors that confer immortality on a cell, even though the specification fails to describe any other species of the genus by structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between structure and function, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus.

In response, but without conceding the correctness thereof, applicant notes that claim 10 has been canceled. Thus, the Examiner's rejection of this claim is now moot.

In response to the rejection of claims 1, 3-5, 8-9 and 12, without conceding the correctness of the Examiner's position, applicant notes that amended claims 1 and 8 contain language which fully addresses the Examiner's stated concern. Thus, the Examiner's remarks are inapposite to the claims as amended, and the inventor had possession of the claimed invention at the time the instant application was filed.

In view of the above remarks, applicant maintains that claims 1, 3-5, 8-9 and 12 satisfy the requirements of 35 U.S.C. §112, first paragraph.

Claim Rejections under 35 U.S.C. §102(b)

The Examiner rejected claims 1 and 3-5 under 35 U.S.C. §102(b) as allegedly anticipated by Wang et al. (In Vitro Cellular and Developmental Biology 27(1): 63-74, 1/1991).

In response, applicant respectfully traverses the Examiner's rejection.

Claim 1 provides an immortalized human cardiomyocyte cell line. The claimed cell line is produced by a method comprising the step of fusing a post-mitotic primary non-immortalized human cardiomyocyte with a human fibroblast. The fibroblast has the features of having been treated with ethidium bromide, comprising a replicable vector expressing SV40 large T antigen which confers immortality on a cell comprising same, and being free of mitochondrial DNA. Claims 3-5 provide specific embodiments of the cell line of claim 1.

According to M.P.E.P. §2131.01, "[a] claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." Thus, for Wang et al. to anticipate the cell line of claims 1 and 3-5, it would have to teach each and every element thereof. Wang et al. fails to do this since it teaches a different production methodology to the one detailed in claims 1 and 3-5. Specifically, Wang et al. teaches a human fetal cardiac myocyte cell line that is produced by cotransfecting fetal cardiac myocytes with the plasmids pSV2Neo and pRSVTAg, using the calcium phosphate

procedure. (See pages 63 [abstract] and 64). Nowhere in Wang et al. does the reference teach a production method using a human fibroblast having been treated with ethidium bromide, comprising a replicable vector expressing SV40 large T antigen, and being free of mitochondrial DNA. The Examiner has not set forth any reference which would suggest that the claimed cell line and that of Wang et al. are the same, notwithstanding the different production methods used.

Accordingly, Wang et al. fails to anticipate the cell line of claims 1 and 3-5, and the Examiner has not established any teaching to the contrary.

In view of the above remarks, applicant maintains that claims 1 and 3-5 satisfy the requirements of 35 U.S.C. §102(b).

Supplemental Information Disclosure Statement

In accordance with the duty of disclosure under 37 C.F.R. §1.56, applicant would like to direct the Examiner's attention to the following disclosures, which are listed on Form PTO-1449 (**EXHIBIT A**). Copies to the disclosures listed below as items 1-2 are attached hereto as **EXHIBITS 1** and **2**, respectively.

1. DeCaprio, J.A., "The role of J domain of SV40 large T antigen in cellular transformation." Biologicals, 27:23-28 (1999); and

2. Fire, A., et al., "Potent and specific genetic interference by double-stranded RNA in *Caenorhabditis elegans*." Nature, 391:806-811 (1998).

Pursuant to 37 C.F.R. §1.97(c)(2), the required fee for filing this Supplemental Information Disclosure Statement is ONE-HUNDRED AND EIGHTY DOLLARS ($180.00), and a check including this amount is enclosed.

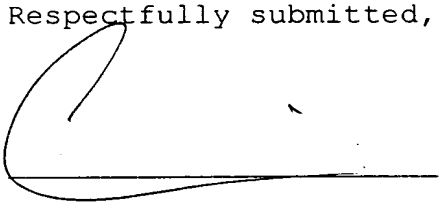
Summary

Applicant maintains that the claims pending are in condition for allowance. Accordingly, allowance is respectfully requested.

If a telephone conference would be of assistance in advancing prosecution of the subject application, applicant's undersigned attorney invites the Examiner to telephone him at the number provided below.

No fee, other than the enclosed sum of $655.00, which includes the $475.00 fee for a three-month extension of time and the $180.00 fee for filing a Supplemental Information Disclosure Statement, is deemed necessary in connection with the filing of this Amendment. However, if any additional fee is required, authorization is hereby given to charge the amount of such fee to Deposit Account No. 03-3125.

Respectfully submitted,



John P. White
Registration No. 28,678
Alan J. Morrison
Registration No. 37,399
Attorneys for Applicant
Cooper & Dunham LLP
1185 Avenue of the Americas
New York, New York 10036
(212) 278-0400

I hereby certify that this correspondence is being deposited this date with the U.S. Postal Service with sufficient postage as first class mail in an envelope addressed to:
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

10/10/03
Alan J. Morrison — Date
Reg. No. 37,399